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EXAMINER

WILDER, CYNTHIA B

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|------------------------------------|--|
| Office Action Summary | Application No. 10/719,372 | Applicant(s) DAHL ET AL. | |
| | Examiner CYNTHIA B. WILDER | Art Unit 1637 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 March 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 172-197 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 172-197 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's amendment filed 3/19/2008 is acknowledged and has been entered. Claims 1-171 and 198-205 have been canceled. Claims 172-197 are pending and addressed in this Office action. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejections

3. The prior art rejection under 35 USC 102(b) and 102(e) and 103(a) are maintained and discussed below.

Claim Rejections - 35 USC § 102(b)

4. Claims 172 and 174 are rejected under 35 U.S.C. 102(b) as being anticipated by Kacian et al (5,399,491, March 1995). Kacian et al teach a method for making a transcription product having a sequence corresponding to a target sequence in a target nucleic acid in a sample, the method comprising the steps of: (a) obtaining an RNA polymerase that can transcribe RNA using a single-stranded promoter; (b) obtaining single-stranded DNA comprising the target sequence that is present in or complementary to a sequence in the target nucleic acid in the sample; (c) operably joining to the single-stranded DNA a single-stranded polynucleotide comprising a promoter that binds the RNA polymerase, thereby obtaining a single-stranded transcription substrate; (d) obtaining nucleoside triphosphates (NTPs) that are substrates for the RNA polymerase and that are complementary to canonical nucleic acid bases; admixing the RNA polymerase, the single-stranded transcription substrate and the NTPs; (e) and (f) incubating the RNA polymerase, the single-stranded transcription substrate and the NTPs to synthesize the transcription product (col. 4-8). Regarding claim 174, Kacian et al teach wherein the single-stranded DNA comprising the target sequence is obtained using a target nucleic acid comprising: (a) DNA; (b) or RNA (col. 6, lines 13-20).

Claim Rejections - 35 USC § 102(e)

5. Claims 172 and 174 are rejected under 35 U.S.C. 102(e) as being anticipated by Kurn et al (20020058270, effective filing June 26, 2000). Regarding claim 172, Kurn et al teach a method for

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making a transcription product having a sequence corresponding to a target sequence in a target nucleic acid in a sample, the method comprising the steps of: (a) obtaining an RNA polymerase that can transcribe RNA using a single-stranded promoter; (b) obtaining single-stranded DNA comprising the target sequence that is present in or complementary to a sequence in the target nucleic acid in the sample; (c) operably joining to the single-stranded DNA a single-stranded polynucleotide comprising a promoter that binds the RNA polymerase, thereby obtaining a single-stranded transcription substrate; (d) obtaining nucleoside triphosphates (NTPs) that are substrates for the RNA polymerase and that are complementary to canonical nucleic acid bases; admixing the RNA polymerase, the single-stranded transcription substrate and the NTPs; (e) and (f) incubating the RNA polymerase, the single-stranded transcription substrate and the NTPs to synthesize the transcription product (0053, 0067, 0076, 0099, 0100, 0107-0112).

Regarding claim 174, Kurn et al teach wherein the single-stranded DNA comprising the target sequence is obtained using a target nucleic acid comprising: (a) DNA; (b) at least one mRNA; or (c) substantially all mRNA in a sample (0161).

Claim Rejections - 35 USC § 103(a)

6. Claims 173 and 175-186, 194 and 195 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kurn et al as previously applied in view Kacian et al as previously applied above and further in view of Ginsberg et al (citation made of record on IDS 6/24/2006).

Regarding claim 173, Kurn et al teach a method as previously described above. Kurn et al further teach additional steps or repetition of second set of transcription steps using the sense strand of final process steps from the first transcription as the starting substrate which results in exponential amplification of the sequence of interest or second transcription product (see 0050, 0067 and 0100). Kurn et al teach wherein the method may utilize an RNA-dependent DNA polymerase such as reverse transcriptase (0142) in the formation of single stranded cDNA from a primer-RNA complex (0023 and 0024).

Kacian et al teach a method similar to that of Kacian et al for making a transcription product. Kacian et al teach the use of reverse transcriptase for synthesizing a cDNA from the initially synthesized cDNA strand (see col. 45-46, section F).

However, MPEP 2144.04 notes, "selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results".

Nonetheless, Ginsberg et al teach a method of making a transcription product having a sequence corresponding to a target sequence in a target nucleic acid sample, wherein the method comprises the additional steps of obtaining a reverse transcriptase, reverse transcribing the transcription product to obtain a first strand cDNA complementary to the transcription product and incubating the first strand cDNA product in the presence of a single stranded polynucleotide comprising a promoter that binds to an RNA polymerase, mixing and incubating the RNA polymerase, the single stranded transcription substrate and NTPs to synthesize a second transcription product (0020-0026, 0030-0036 and especially 0044). Ginsberg et al teach that the method is highly efficient with improved sensitivity (see 0023). Therefore, in view of the foregoing, it would be predictable to one of ordinary skill in the art at the time of the claimed invention multiple products as produced by the transcription method of Kurn et al can be synthesized efficiently to produce additional products corresponding to the target sequence as taught by Kacian et al and Ginsberg et al.

Regarding claim 175, Kacian et al teach wherein the single-stranded transcription substrate of step (c) is obtained by primer extension of the single-stranded DNA of step (b) using a promoter splice template oligo annealed to the 3'-end of the single-stranded DNA as a template, said splice template oligo comprising: (a) a 5'-end portion that is complementary to a desired sequence to be added to the 3'-end of the first-strand cDNA; and (b) a 3'-end portion that is complementary to the 3'-end of the first-strand cDNA, wherein the 3'-terminus is blocked so it cannot be primer extended using a DNA polymerase (col. 4, 7 and col. 14)..

Regarding claim 176, Kacian et al teach wherein the 5'-end portion of said splice template oligo is complementary to part of or all of a sense or an anti-sense promoter sequence for an RNA polymerase that can bind a single-stranded promoter (col. 7 and col. 13).

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Regarding claim 177, Kacian et al teach wherein the single-stranded DNA is obtained by reverse transcription of a transcription product (col. 8, lines 40-48 and col. 45, section F).

Regarding claims 178-186, Kacian et al teach wherein the method comprise the sub-steps of: (a1) obtaining a primer for synthesis of a first-strand cDNA, the primer comprising a sequence complementary to the sequence at the 3'-end of the target sequence to be transcribed; (b1) annealing the primer to the target nucleic acid; (c1) primer-extending the primer annealed to the target nucleic acid with a DNA polymerase to obtain a linear first-strand cDNA comprising a sequence complementary to the target sequence; (d1) obtaining a promoter splice template oligo comprising: (i) a 3'-end that is sufficiently homologous to the 3'-end of the linear first-strand cDNA, including the tail if present, to hybridize therewith, and that is blocked so that it cannot itself be primer-extended by a DNA polymerase; and (ii) a 5'-portion that exhibits a sequence that is complementary to a transcription promoter for an RNA polymerase that can synthesize RNA using a single-stranded transcription substrate; (e1) annealing the promoter splice template oligo to the linear first-strand cDNA including the tail if present; (f1) primer-extending the linear first-strand cDNA including the tail, if present, with a DNA polymerase to obtain a promoter-containing linear first-strand cDNA that has a 3'-portion that is complementary to the portion of the promoter splice template oligo that is not hybridizable to the first-strand cDNA including the tail, if present; and (g1) removing or dissociating the promoter splice template oligo from the promoter-containing linear first-strand cDNA to obtain the single-stranded transcription substrate. Kacian et al additionally teach wherein the method comprises (a2) obtaining a blocking oligo, the blocking oligo comprising a sequence that anneals to the target nucleic acid so as to delimit the 3'-end of a primer extension product of the primer using the target nucleic acid as a template, wherein the blocking oligo is not displaced by the primer extension product, and wherein the blocking oligo is not itself capable of being primer-extended by a DNA polymerase; and (b2) annealing the blocking oligo, together with the primer, to the target nucleic acid in step (b1) prior to primer-extending the primer in step (c1) (cols. 4-8, 21 and 45). Kacian et al teach removal of the original target using RNase H (col. 31, lines 27-30).

In regards to the limitation concerning the selection of the primer for synthesis of a linear first strand cDNA, Kurn et al teaches wherein a random primer may be used for synthesis of a liner cDNA strand (paragraphs 0072 and 0186).

In regards to the limitation wherein a tail is added to the first strand cDNA, Ginsberg et al teach this limitation (Figure 9). In regards to the order of method steps as recited in the rejected claims, it is noted that MPEP 2144.04 notes "selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results".

Regarding claim 194, Ginsberg et al teach wherein the target has a tail sequence comprising at least two nucleotides (see figure 9)

Regarding claim 195, Kurn et al teach wherein at least one of the NTP comprise 2-fluoro- or 2-azido (see 0066).

7. Claims 187-193, 196 and 197 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kurn et al and Kacian et al and further in view of Ginsberg et al as previously applied above and further in view of Diegelman et al (nucleic acids Research, vol. 26, no. 13, pages 3235-3241, 1998). Regarding claims 187-193, 196 and 197, Kurn et al in view of Kacian in view of Ginsberg et al teach a method for making a transcription product having a sequence corresponding to a target sequence as previously applied above. The references however do not teach the steps of circularizing the antisense promoter with a ligase and obtaining a circular single stranded transcription substrate. Likewise, the references do not teach the use of a ligation splint or wherein the transcription product comprises a hairpin RNA. However, Kurn et al do teach the formation of hairpin loop via self-ligation (see 0071).

Diegelman et al teach a method for the in vitro synthesis of circular RNA and formation of hairpin transcription products. Diegelman et al teach wherein ligation conditions comprises using a ligation splint, addition of a ligase in the presence of a T7 RNA polymerase (see "Material and Methods, page 3225, col. 2 to page 3226 col. 1). Diegelman et al teach this method can be successful in producing amplified amounts of both circular and linear hairpin (see 3239, col. 2). Diegelman et al teach that this rolling circle strategy may be useful for the generation of certain biological relevant RNAs (page 3240, col. 2). Therefore, in view of foregoing, it would be obvious to one of ordinary skill in the art at the time of the

claimed invention that a rolling circle strategy can successfully result in the making of a transcription product as suggested by Diegelman et al.

Response to Arguments

8. Applicant traverses the rejection on the following ground: Applicant states none of the cited references teach or suggest formation of a single stranded transcription substrate by joining a single stranded polynucleotide comprising a promoter to a single stranded DNA comprising the target sequence. Applicant also objects to the Examiner's interpretation of the claims.

9. All of the arguments have been thoroughly reviewed and considered but are not found persuasive. In response to Applicant's arguments that the cited prior art does not teach the limitation recited above, the examiner respectfully disagree. Kacian teaches joining a single a single stranded polynucleotide comprising a promoter to a single stranded to a single stranded DNA comprising the target (see e.g., column 4, line 34 to column 5, line 19 and col. 13 and entire patent). Kurn et al also meets this limitation (see e.g., see entire patent especially paragraphs 0318-0322). With regards applicant's assertion with respect to the Examiner's interpretation of the claims, it is noted that the courts have established that during patent examination the pending claims must be interpreted as broadly as their terms reasonably allow (*In re Zletz*, 893 F.2d 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989). In this case, the claims recited the transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., > Mars Inc. v. H.J. Heinz Co., 377 F.3d

1369, 1376, 71 USPQ2d 1837, 1843 (Fed. Cir. 2004). Neither the specification nor claims exclude rolling circle strategies in the in vitro transcription techniques claimed. It is determined that the Examiner's broad interpretation of the claims is valid.

Conclusion

10. No claims are allowed. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CBW/

/GARY BENZION/

Supervisory Patent Examiner, Art Unit 1637